

isolating the betulonic aldehyde.

22
11.

(Amended) A method of preparing betulonic aldehyde comprising:
reacting betulinol with chromium anhydride in acetone in the presence
of sulfuric acid for a time and under conditions effective to produce a reaction mixture that
includes betulonic aldehyde;

cooling the reaction mixture;

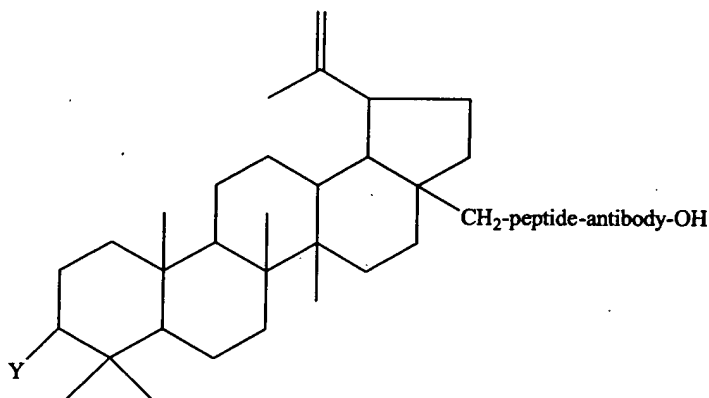
adding water to the reaction mixture, whereby a sediment containing
betulonic aldehyde forms;

crystallizing the sediment; and

isolating the betulonic aldehyde.

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11.

(Twice-Amended) A method of producing a betulinol-antibody
conjugate having the formula:



wherein

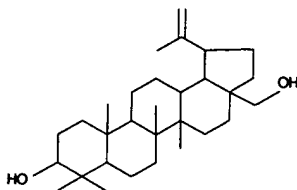
Y is a hydroxy group, an alkoxy group, or an alkanoyloxy
group,

said method comprising:

wherein R is alkyl,

said method comprising:

alkylating a dialcohol having the formula:



with a nitrile having the formula:



for a time and under conditions effective to form the diether, and
isolating the diether.

comprising:

oxidizing betulinol with chromium anhydride in acetone in the
presence of sulfuric acid for a time and under conditions effective to produce betulonic
aldehyde, and

isolating the betulonic aldehyde.

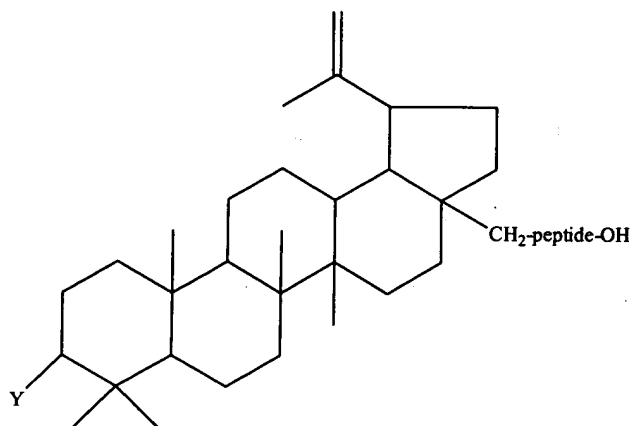
comprising:

reacting betulinol with chromium anhydride in acetone in the presence
of sulfuric acid for a time and under conditions effective to produce a reaction mixture that
includes betulonic aldehyde;

cooling the reaction mixture;

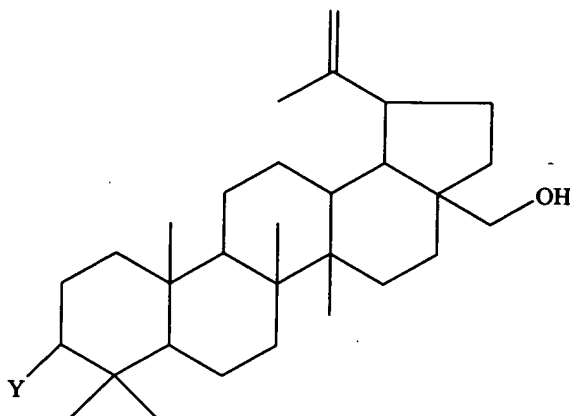
adding water to the reaction mixture, whereby a sediment containing
betulonic aldehyde forms; and

reacting a betulinol peptide having the formula:



with an antibody having the formula H-antibody-OH for a time and under conditions effective to produce the betulinol-antibody conjugate, and isolating the betulinol-antibody conjugate.

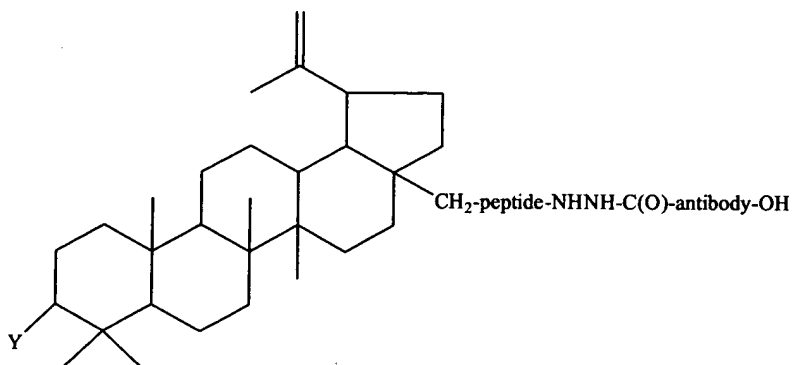
28 22. (Twice-Amended) 23 A method according to claim 17, wherein said betulinol peptide is obtained by a process comprising:
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reacting a compound having the formula:



with a peptide having the formula H-peptide-OH for a time and under conditions effective to produce the betulinol peptide, and isolating the betulinol peptide.

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23.

(Twice-Amended) A method of producing a betulinol-antibody conjugate having the formula:

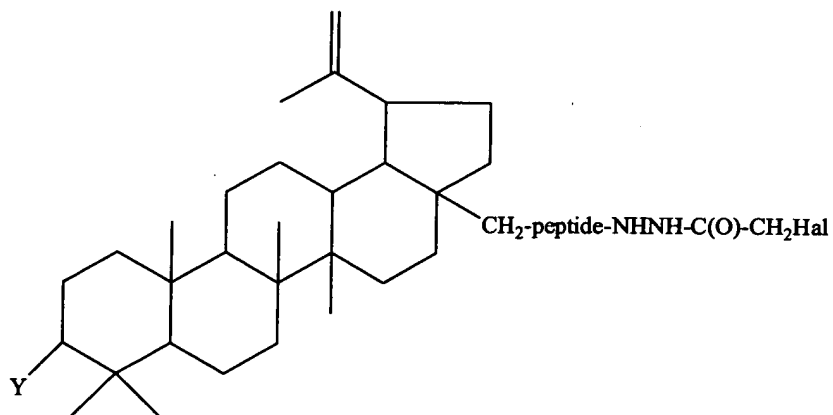


wherein

Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group,

said method comprising:

reacting a haloacetylhydrazide having the formula:

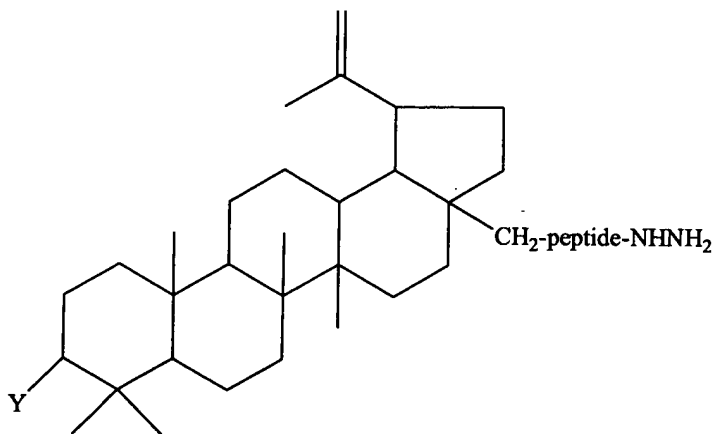


wherein

Hal is a halogen

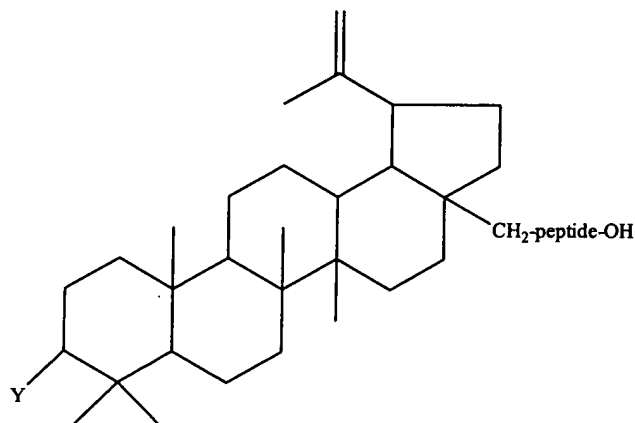
with an antibody having the formula H-antibody-OH for a time and under conditions effective to produce the betulinol-antibody conjugate, and
isolating the betulinol-antibody conjugate.

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~~29~~. (Twice-Amended) A method according to claim ²⁹~~23~~, wherein said haloacetylhydrazide is obtained by a process comprising:
reacting a hydrazide having the formula:



with a *para*-nitrophenyl α -haloacetate for a time and under conditions effective to produce the haloacetylhydrazide, and
isolating the haloacetylhydrazide.

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~~30~~. (Twice-Amended) A method according to claim ³⁵~~29~~, wherein said hydrazide is obtained by a process comprising:
reacting a betulinol peptide having the formula:

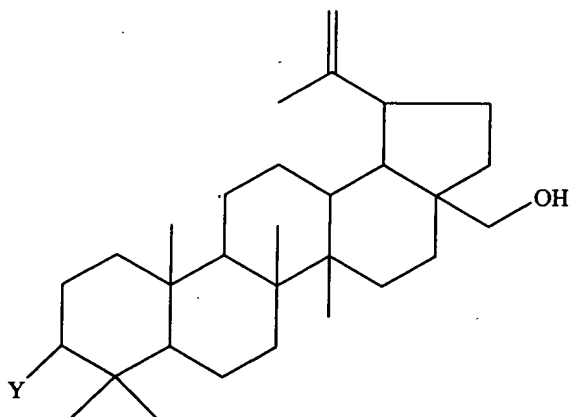


with hydrazine hydrate for a time and under conditions effective to produce the hydrazide,
and
isolating the hydrazide.

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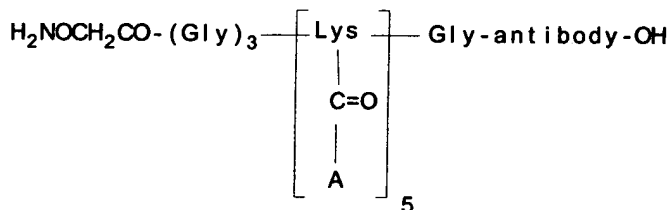
31. (Twice-Amended) A method according to claim 30, wherein said betulinol peptide is obtained by a process comprising:
reacting a compound having the formula:



with a peptide having the formula H-peptide-OH for a time and under conditions effective to produce the betulinol peptide, and
isolating the betulinol peptide.

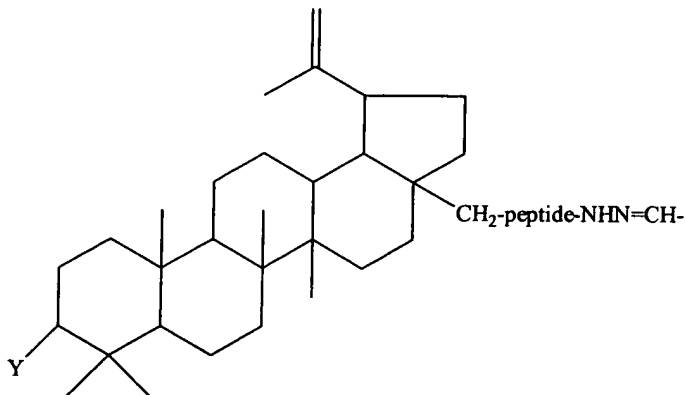
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33. (Twice-Amended) A method of producing a betulinol-antibody conjugate having the formula:



wherein

each "A" moiety is independently selected from the group consisting of a -CHO group and a moiety having the formula:



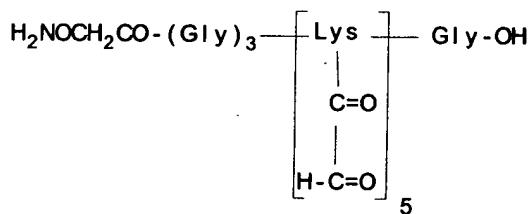
provided that at least one of A is not -CHO; and

Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group,

said method comprising:

reacting a carrier molecule having the formula:

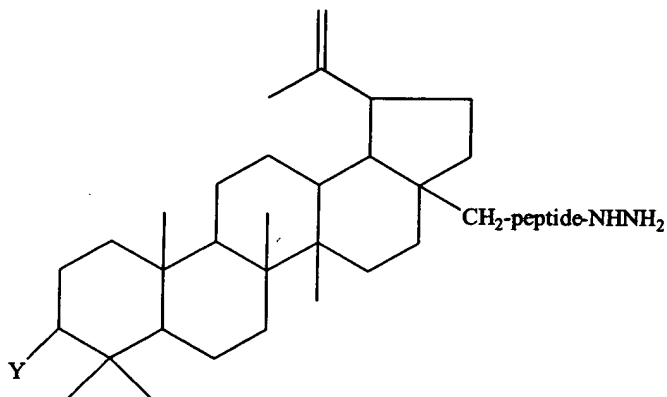
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a hydrazide having the formula:

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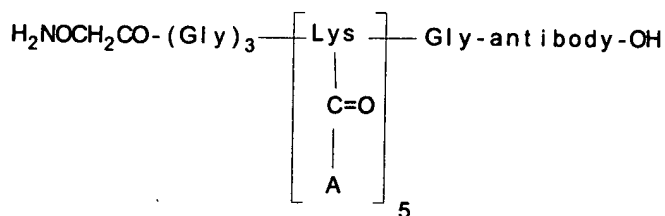
and an antibody having the formula H-antibody-OH for a time and under conditions effective to produce the betulinol-antibody conjugate, and

isolating the betulinol-antibody conjugate.

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(Twice-Amended) A method of producing a betulinol-antibody conjugate having the formula:

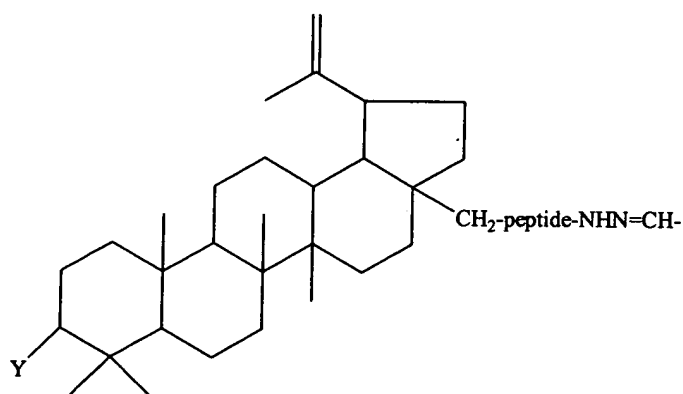
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wherein

each "A" moiety is independently selected from the group consisting of a -CHO group and a moiety having the formula:

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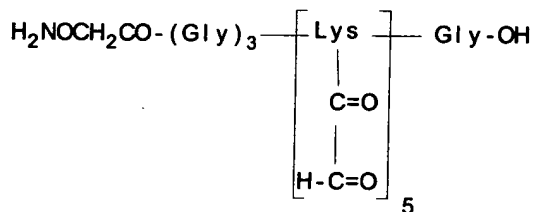
provided that at least one of A is not -CHO; and

Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group,

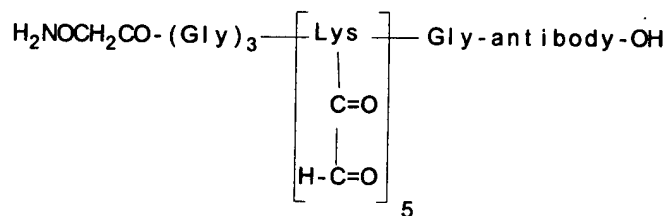
said method comprising:

reacting a carrier molecule having the formula:

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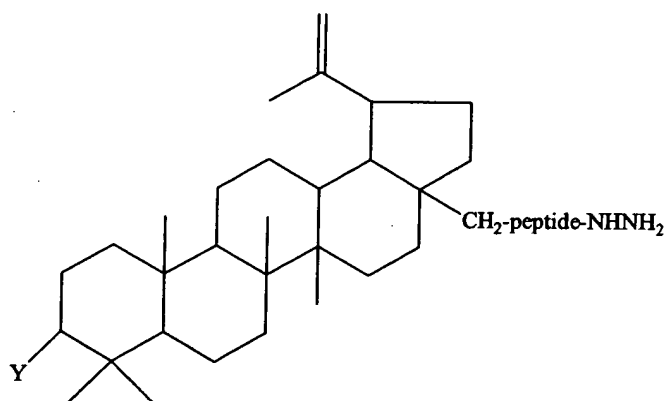
with an antibody having the formula H-antibody-OH for a time and under conditions effective to produce an antibody-bound carrier molecule having the formula:



and

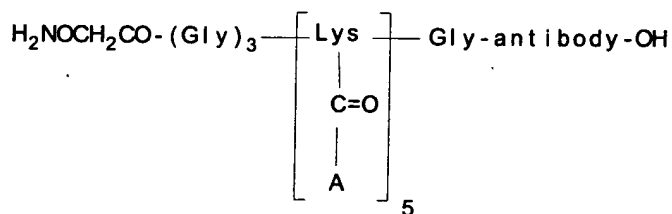
the formula:

reacting the antibody-bound carrier molecule with a hydrazide having



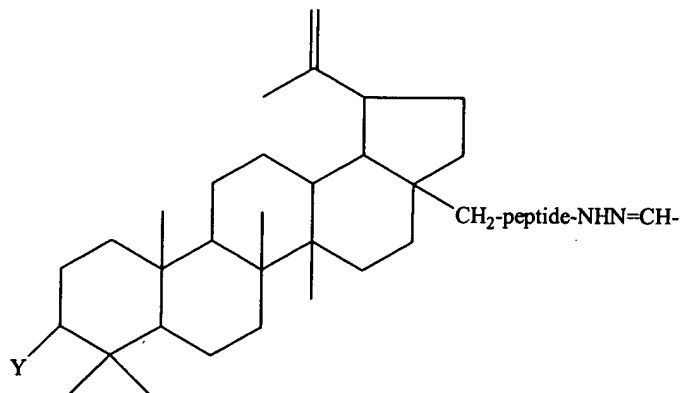
for a time and under conditions effective to produce the betulinol-antibody conjugate, and isolating the betulinol-antibody conjugate.

35. (Twice-Amended) A method of producing a betulinol-antibody conjugate having the formula:



wherein

each "A" moiety is independently selected from the group consisting of a -CHO group and a moiety having the formula:

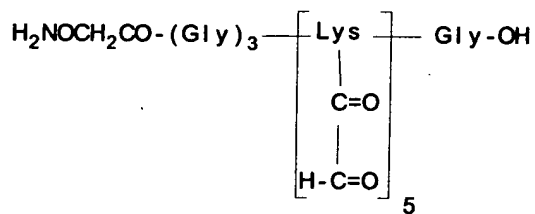


provided that at least one of A is not -CHO; and

Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group,

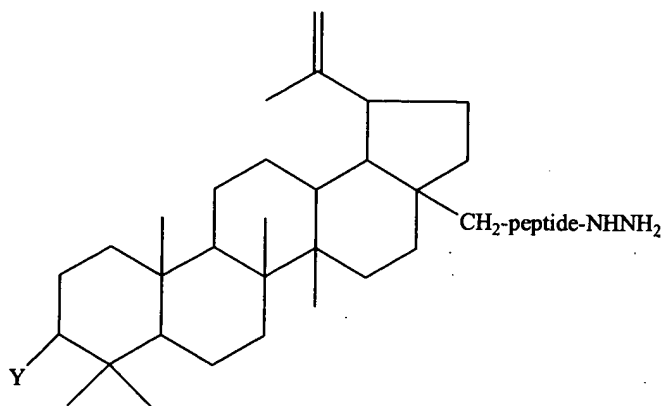
said method comprising:

reacting a carrier molecule having the formula:



with a hydrazide having the formula:

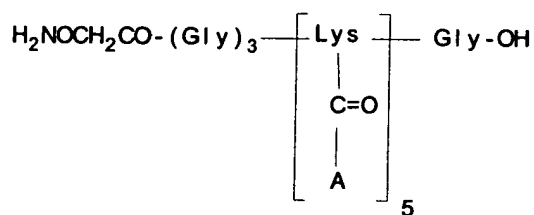
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for a time and under conditions effective to produce a betulinol-bound carrier molecule having the formula:

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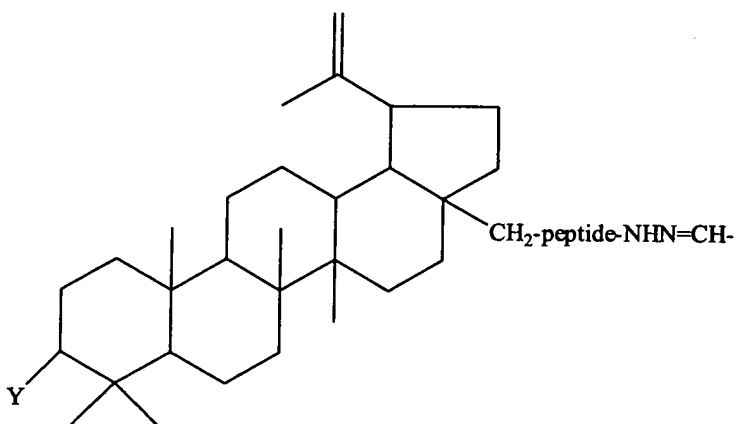
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wherein

at least one A is a moiety having the formula:

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and

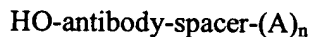
reacting the betulinol-bound carrier molecule with an antibody having the formula H-antibody-OH for a time and under conditions effective to produce the betulinol-antibody conjugate, and

isolating the betulinol-antibody conjugate.

formula:

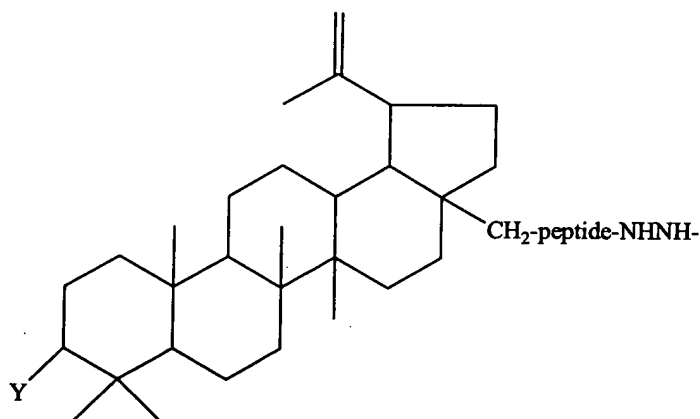
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36.

(Twice-Amended) A betulinol-antibody conjugate having the



wherein

A is a moiety having the formula:



Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group;

"spacer" is multivalent moiety bonded to the antibody and (A)_n;

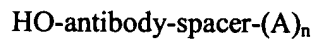
and

n is an integer from 1 to 100.

9 36. (Twice-Amended) A betulinol-antibody conjugate according to claim 36, wherein "spacer" is a multivalent moiety produced from a diamine derivative of polyethylene glycol having 2-(pyridyldithio)-propionyl and N-hydroxysuccinimide ester groups bonded thereto.

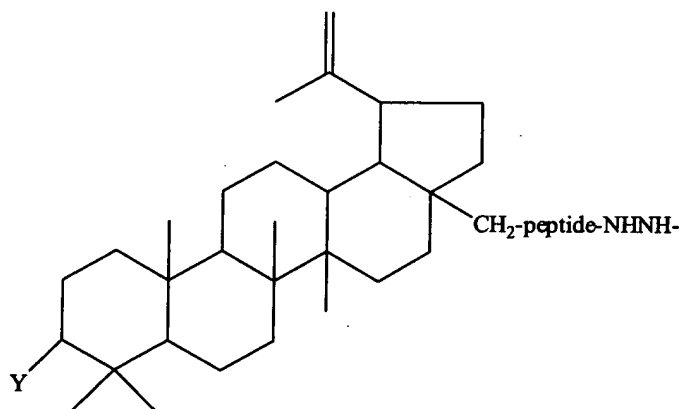
9 36. (Twice-Amended) A betulinol-antibody conjugate according to claim 36, wherein "spacer" is a multivalent moiety produced from a branched form of polyethylene glycol propionic acid N-hydroxysuccinimide ester.

41. (Twice-Amended) A method of producing a betulinol-antibody conjugate having the formula:



wherein

A is a moiety having the formula:



Y is a hydroxy group, an alkoxy group, or an alkanoyloxy group;

"spacer" is multivalent moiety bonded to the antibody and (A)_n;

and

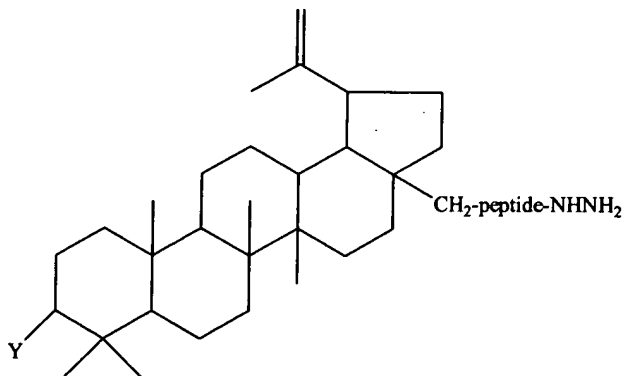
n is an integer from 1 to 100,

said method comprising:

providing a "spacer" having a first reactive terminus and one or more second reactive termini;

reacting an antibody with the first reactive terminus;

reacting a hydrazide having the formula:



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with one or more of the one or more second reactive termini for a time and under conditions effective to produce the betulinol-antibody conjugate; and
isolating the betulinol-antibody conjugate.

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45. (Twice-Amended) A method according to claim 41, wherein
"spacer" is a multivalent moiety produced from a diamine derivative of polyethylene glycol having 2-(pyridyldithio)-propionyl and N-hydroxysuccinimide ester groups bonded thereto.

46. (Twice-Amended) A method according to claim 41, wherein
"spacer" is a multivalent moiety produced from a branched form of polyethylene glycol propionic acid N-hydroxysuccinimide ester.
